Gold-catalyzed heterocyclizations in alkynyl- and allenyl-β-lactams

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Abstract

New gold-catalyzed methods using the β-lactam scaffold have been recently developed for the synthesis of different sized heterocycles. This overview focuses on heterocyclization reactions on allenic and alkynic β-lactams relying on the activation of the allene and alkyne component, accounting for the mechanism, as well as for the regio- and stereoselectivity of the cyclizations.

Keywords

alkynes; allenes; gold; heterocyclizations; β-lactams

Introduction

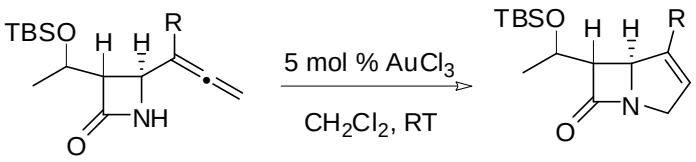
The chemistry of alkynes and allenes has been extensively studied and many reviews on their preparation and reactivities have been published [1–9]. They have shown an interesting reactivity and selectivity affording complex structures in a limited number of steps. The last decade has witnessed dramatic growth in the number of reactions catalyzed by gold complexes because of their powerful soft Lewis acidic nature [10–16]. In particular, gold-catalyzed intramolecular addition of oxygen and nitrogen nucleophiles across an allene or a carbon–carbon triple bond is intriguing from the point of view of regioselectivity (*endo* versus *exo* cyclizations) as well as it being one of the most rapid and convenient methods for the preparation of heterocycles. On the other hand, in addition of the key role that β-lactams have played in medicinal chemistry, namely, the fight against pathogenic bacteria, enzyme inhibition, or gene activation [17–23], the use of 2-azetidinones as chiral building blocks in organic synthesis is now well established [24–28]. Besides, the cyclic 2-azetidinone skeleton has been extensively used as a template on which to build the carbo(hetero)cyclic structure joined to the four-membered ring, using the chirality and functionalization of the β-lactam ring as a stereocontrolling element [29–30]. This overview focuses on gold-catalyzed heterocyclization reactions on allenic and alkynic β-lactams relying on the activation of the allene and alkyne component, accounting for the mechanism, as well as for the regio- and stereoselectivity of the cyclizations.

Review

Gold-catalyzed heterocyclizations in allenyl-β-lactams

Aminocyclizations

The $AuCl_3$-catalyzed cyclization of 4-allenyl-2-azetidinones afforded bicyclic β-lactams [31], while the selective introduction of the allenyl group at the C4-position of 2-azetidinones was accomplished with the help of organoindium reagents. The best results among the several reaction conditions examined for the incorporation of the allene moiety in the four-membered ring, were obtained with the organoindium reagent that was generated in situ from the reaction of 2.0 equivalents of indium with 3.0 equivalents of substituted propargyl bromide in the presence of 3.0 equivalents of KI; DMF was found to be the best solvent from those that were screened (DMF, THF, C_6H_6, and $C_6H_5CH_3$). Because further functionalization of the allene group could potentially lead to the construction of the bicyclic nucleus, an especially intriguing and fundamental problem in the field of carbapenem synthesis, efforts were devoted to the aminocyclization of 4-(1′-methylallenyl)-2-azetidinone derivatives with a variety of catalysts. Although many palladium-based catalysts such as $Pd(OAc)_2$, $PdCl_2$, $[Pd(PPh_3)_4]$, and $[Pd_2(dba)_3]\cdot CHCl_3$ failed to give the desired cyclized products, exposure of allenyl-β-lactams **1** to 5 mol % $AuCl_3$ in CH_2Cl_2 produced the bicyclic β-lactam products **2** of the Δ^1-carbapenem class (Scheme 1). The desired products were produced in good yields for 2-azetidinones with *n*-butyl, $THPOCH_2$, phenyl, and 2-naphthyl substituents. It should be mentioned that the cyclization of allenyl β-lactams **1** is an application of the gold-catalyzed cycloisomerization of α-aminoallenes which was discovered earlier [32–33].

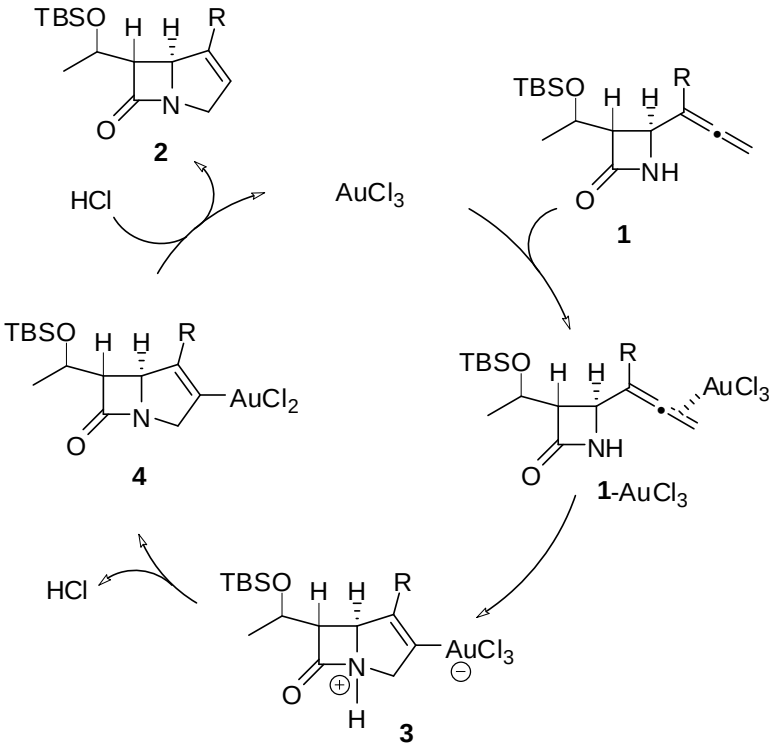


1 **2** (65–85%)

R = Me, Bu, Ph, 2-napthyl, $THPOCH_2$

Scheme 1: Gold-catalyzed cyclization of 4-allenyl-2-azetidinones for the preparation of bicyclic β-lactams.

Although the mechanism of the cyclization reaction has not been fully established, a possible reaction pathway has been proposed (Scheme 2). $AuCl_3$ activates the allene group of 4-allenyl-2-azetidinones **1** to give **1**-$AuCl_3$, and subsequent cyclization affords **3**, which then gives a vinyl gold intermediate **4** [34–37]. Subsequent protonation of the transient vinyl gold intermediate **4** produces bicyclic β-lactams **2** and regenerates $AuCl_3$ to continue the catalytic cycle.

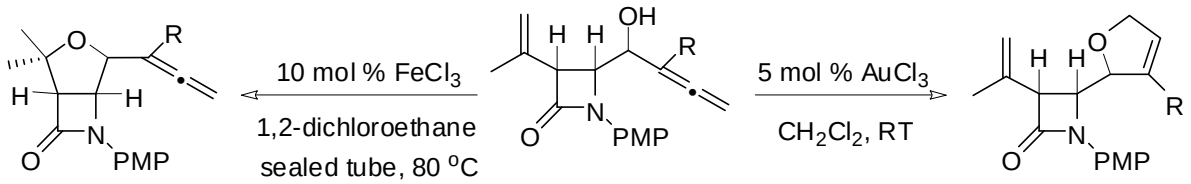


Scheme 2: Possible catalytic cycle for the gold-catalyzed cyclization of 4-allenyl-2-azetidinones.

Oxycyclizations

Furan, tetrahydrofuran, dihydropyran, and oxepane ether rings are ubiquitous structural units that are extensively encountered in a number of biologically active

natural products and functional molecules, and therefore, their stereocontrolled synthesis remains an intensive research area. On the other hand, the recent resplendent age of gold has been accompanied by the emergence of iron salts as powerful alternatives in view of their inexpensiveness and environmental friendliness [38–40]. The chemodivergent metal-catalyzed heterocyclization of alcohols bearing both an allene and an alkene center has been reported [41]. Starting from 2-azetidinone-tethered enallenols **5**, $FeCl_3$ was able to chemospecifically catalyze the cyclization in favour of the alkene component to exclusively afford β-lactam-tetrahydrofuran hybrids **6** in good isolated yields (Scheme 3). Besides total chemocontrol, the reaction was regiospecific and only the five-membered ring ether was formed, without the presence of the isomeric six-membered ring. By contrast, when the cyclization of olefinic α-allenols **5** was catalyzed by gold salts ($AuCl_3$), allene cycloisomerization adducts **7** were afforded as sole isomers (Scheme 3). It should be mentioned that the cyclization of allenyl β-lactams **5** is an application of the gold-catalyzed cycloisomerization of α-hydroxyallenes which was discovered earlier [42–44].

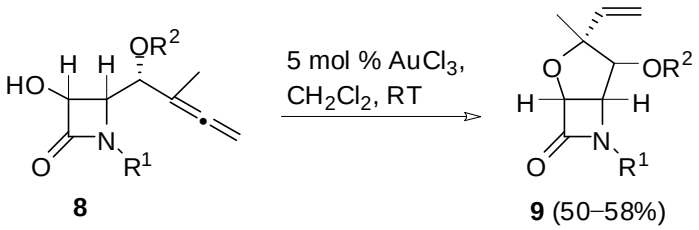


6 (65–83%) **5** **7** (65–84%)

Scheme 3: Gold- and iron-catalyzed chemodivergent cyclization of enallenols for the preparation of oxacyclic β-lactam derivatives.

Similarly to the transition metal-catalyzed reactions of α-allenols leading to heterocyclization products, the intramolecular cyclizations of γ-allenols have also

attracted a great deal of interest [45–47]. A study on the regioselectivity control during the gold-catalyzed O–C functionalization of 2-azetidinone-tethered γ-allenol derivatives has appeared [48–49]. The general reactivity of 2-azetidinone-tethered γ-allenols toward the regioselective hydroalkoxylation reaction was tested with substrate **8a** (R^1 = Bn, R^2 = TBS) by the use of $[PtCl_2(CH_2{=}CH_2)]_2$, $AgNO_3$, AuCl and $AuCl_3$ as catalysts. $[PtCl_2(CH_2{=}CH_2)]_2$ and $AgNO_3$ afforded rather low yield or disappointing diastereomeric mixture of bicycle **9a**. Although $AgNO_3$ was less diastereoselective than $[PtCl_2(CH_2{=}CH_2)]_2$ (60:40 vs 100:0), it was a more efficient catalyst affording adduct **9a** in reasonable yield. Gratifyingly, it was found that Au salts were effective as 5-*exo* selective hydroalkoxylation catalysts. $AuCl_3$ was selected as catalyst of choice because of its superior performance, affording tetrahydrofuran-2-azetidinones **9** in moderate yields (Scheme 4). No regioisomeric products were detected, giving exclusively the fused five-membered oxacycle.



8 **9** (50–58%)

R^1 = Bn, allyl; R^2 = TBS, COPMP

Scheme 4: Gold-catalyzed cyclization of hydroxyallenes for the preparation of five-membered oxacyclic β-lactams. COPMP = O=C-C_6H_4.

A computational study for the above heterocyclization has been carried out [50]. The Au(III)-catalyzed cyclization of γ-allenol **I** (Fig. 1) takes place regio- and stereoselectively through a 5-*exo* hydroalkoxylation because of a kinetic preference governed by electronic and steric factors. A possible pathway for the achievement of bicyclic tetrahydrofurans **9** from γ-allenols **8** may initially involve the formation of a

complex **8**-$AuCl_3$ through coordination of the gold trichloride to the proximal allenic double bond. Next, regioselective 5-*exo* oxyauration forms zwitterionic species **10**. Loss of HCl followed by protonolysis of the carbon–gold bond of **11** affords products **9** and regenerates the gold catalyst (Scheme 5).

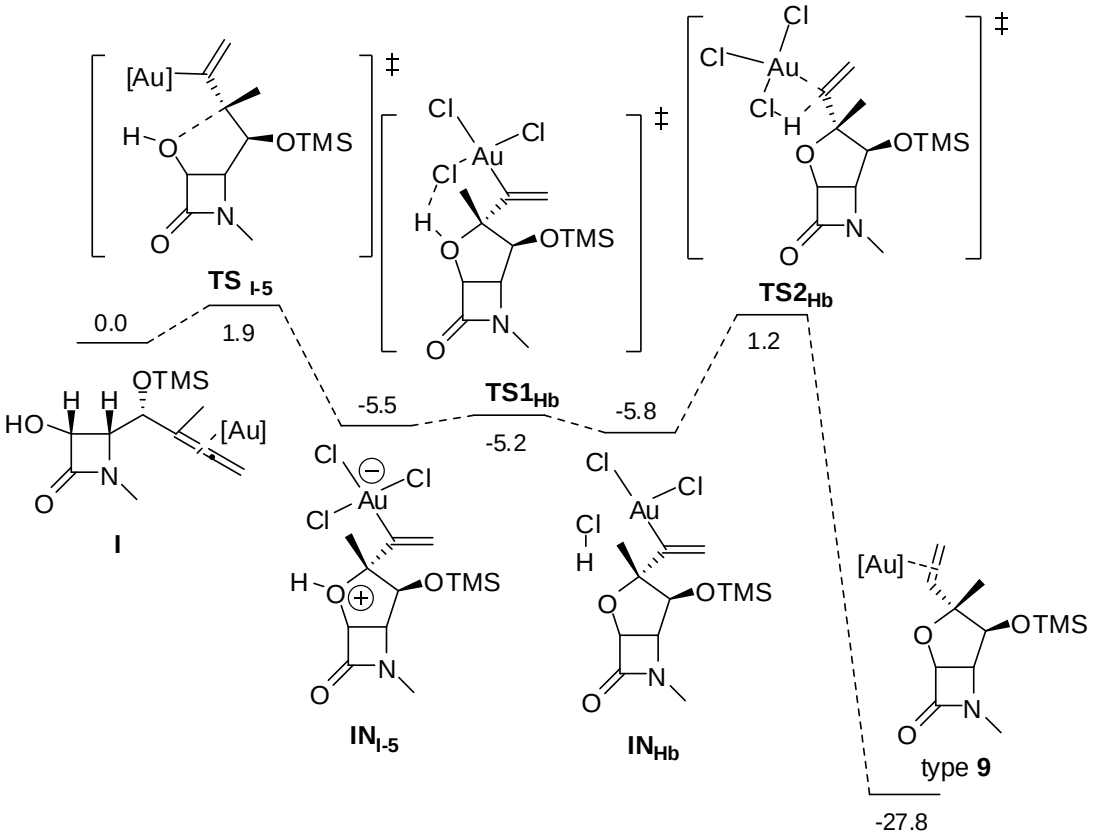
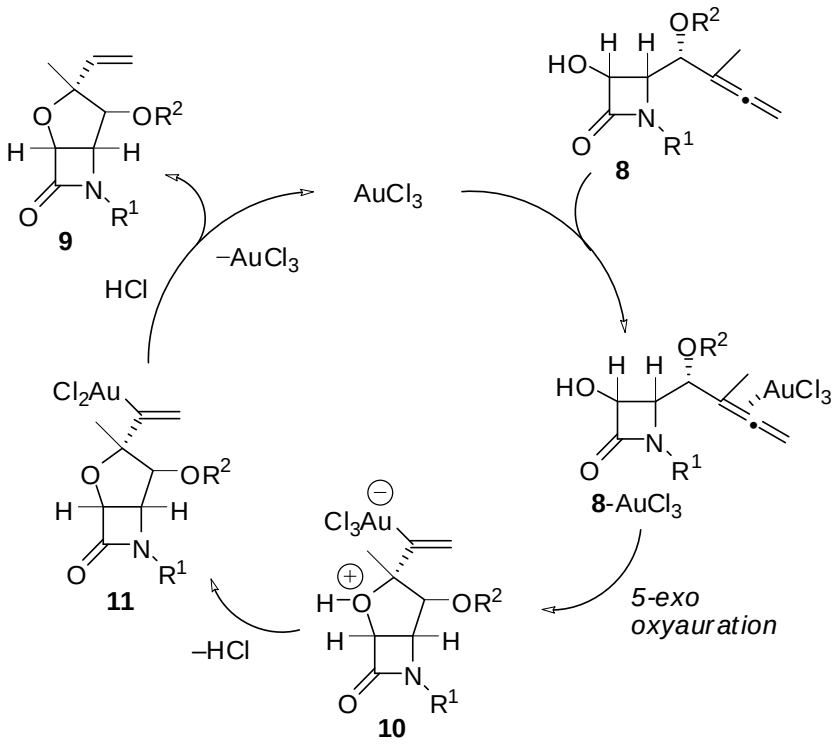


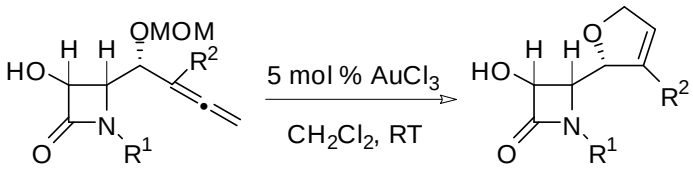
Figure 1: Free energy profile [kcal mol^{-1}] for the transformation of γ-allenol **I** into the tetrahydrofuran type **9**.



Scheme 5: Possible catalytic cycle for the gold-catalyzed cyclization of hydroxyallenes.

Having found a solution for the 5-*exo* selective hydroalkoxylation, it was next examined the more intricate heterocyclizative problem associated with tuning of the regioselectivities of γ-allenol derivatives. It should be mentioned that one of the challenges for modern synthesis is to create distinct types of complex molecules from identical starting materials based solely on catalyst selection. Because the stability of the benzoate and TBS-protective groups to the gold-catalyzed conditions was demonstrated, it was decided to see if (methoxymethyl)oxy substitution has a beneficial impact on the cyclization reactions. In the event, when γ-allenols **12** were treated with $AuCl_3$ the 2,5-dihydrofurans **13** were the sole products (Scheme 6). These transformations may involve a chemoselective (5-*endo-trig* versus 7-*endo-trig*) allenol oxycyclization with concomitant MOM ether deprotection. Taking into account the above results, it was decided to test if the metal-catalyzed preparation of bicycles

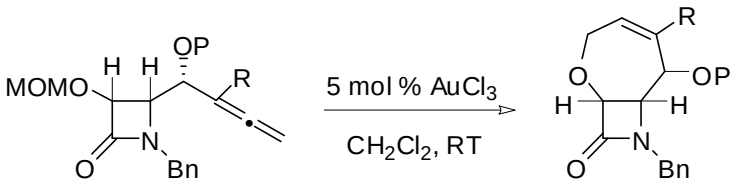
9 can be directly accomplished from MOM protected γ-allenol derivatives **14**. Worhty of note, when allenic MOM ethers **14** were treated with $AuCl_3$, the 5-*exo* mode was completely reverted to a 7-*endo* cyclization to afford bicycles **15** in fair yields (Scheme 7). It seems that the reactivity in this type of Au(III)-catalyzed reactions is determined by the presence or absence of a methoxymethyl protecting group at the γ-allenol oxygen atom, as the free γ-allenols **8** gave 5-*exo* hydroalkoxylation, while MOM protected γ-allenol derivatives **14** exclusively underwent a 7-*endo* oxycyclization. Thus, it has been demonstrated that regioselectivity control in the metal-catalyzed O–C functionalization of γ-allenols can be achieved through the nature of the γ-allenol (free versus protected).



12 **13** (37–53%)

R^1 = Bn, CH_2CO_2Me; R^2 = Me, Ph

Scheme 6: Gold-catalyzed cyclization of MOM-protected α-hydroxyallenes for the preparation of five-membered oxacyclic β-lactams.

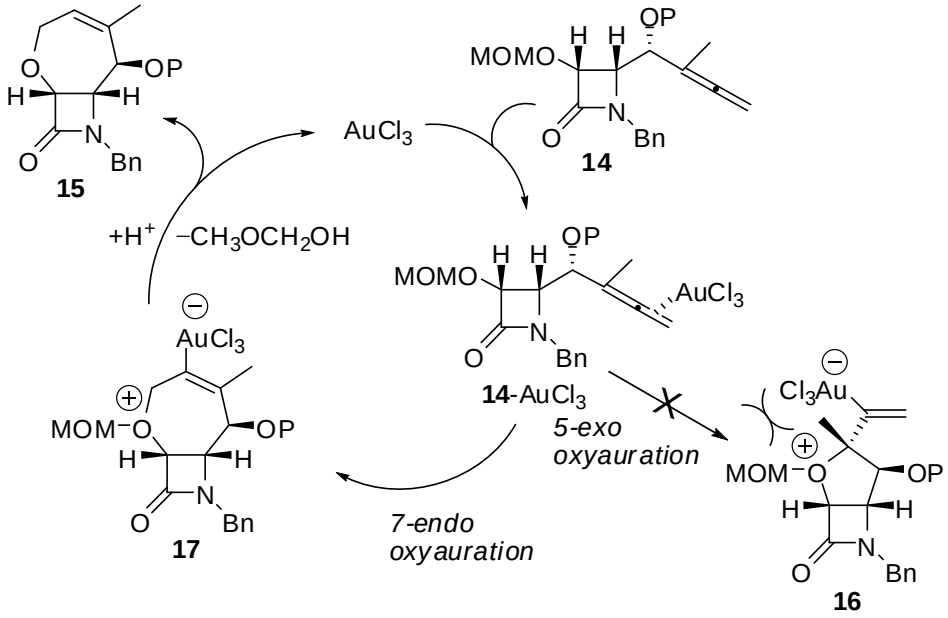


14 **15** (45–75%)

R = Me, Ph P = 4-$MeOC_6H_4CO$, 4-BrC_6H_4CO, MeCO

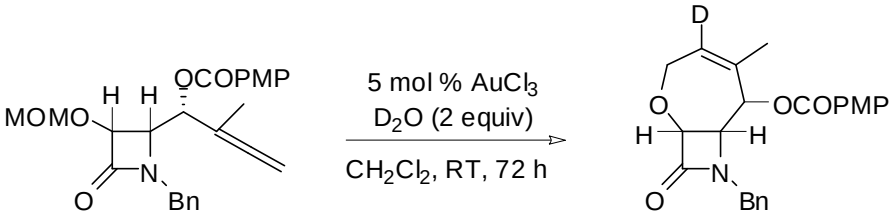
Scheme 7: Gold-catalyzed cyclization of MOM-protected γ-hydroxyallenes for the preparation of seven-membered oxacyclic β-lactams.

The pathway proposed in Scheme 8 looks valid for the formation of products **15** from MOM protected γ-allenol derivatives **14**. It could be presumed that the initially formed allenegold complex **14**-$AuCl_3$ undergoes an intramolecular attack (7-*endo* versus 5-*exo* oxyauration) by the (methoxymethyl)oxy group, giving rise no to species **16** but to the tetrahydrooxepine intermediate **17**. Protonolysis of the carbon–gold bond linked to an elimination of methoxymethanol would then liberate the bicycle type **15** with concomitant regeneration of the Au(III) species. Probably, the proton in the last step of the catalytic cycle comes from the trace amount of water present in the solvent or the catalyst. In the presence of MOM group, 5-*exo* cyclization falters. As calculations reveals, 5-*exo* oxyauration via **16** is restricted by the steric hindrance between the (methoxymethyl)oxy group and the substituents at the quaternary stereocenter.



Scheme 8: Possible catalytic cycle for the gold-catalyzed cyclization of MOM protected γ-allenol derivatives.

With the aim of trapping the organogold intermediate to confirm the mechanism of this reaction, deuterium labeling studies with deuterium oxide were performed. Under the same conditions but with the addition of two equivalents of D_2O, heterocyclization reaction of MOM protected γ-allenol **14a** catalyzed by $AuCl_3$ in dichloromethane afforded [4-D]-**15a** in 48% yield, indicating that a deuterium atom was incorporated at the alkenyl carbon (Scheme 9). The fact that the $AuCl_3$-catalyzed conversion of allenol **14a** into bicycle **15a** in the presence of two equivalents of D_2O afforded [4-D]-**15a**, as judged by the disappearance of the peak at 6.35 ppm in the ^1H NMR spectrum, which is the signal of the proton H4 on the 2-oxa-8-azabicyclo[5.2.0]non-4-en-9-one (**15a**), suggests that deuterolysis of the carbon–gold in species type **17** has occurred. Along with the clarification of the reaction mechanism, it should point out at the same time that, although metal-catalyzed oxycyclization reactions of allenes are well-known in hydroxyallenes, heterocyclizations of alkoxyallenes is not an easy task and still remains a real challenge.



14a **[4-D]-15a** (48%)

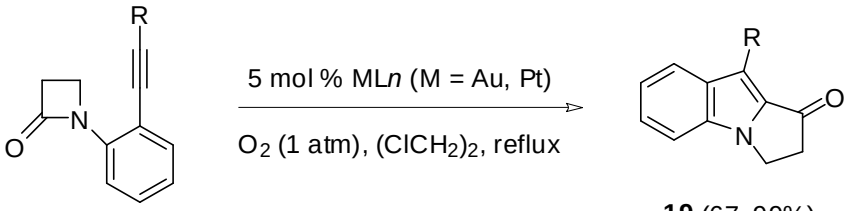
Scheme 9: Au(III)-catalyzed heterocyclization reaction of MOM protected γ-allenol derivative **14a**.

Gold-catalyzed heterocyclizations in alkynyl-β-lactams

Aminocyclizations

The precious metal-catalyzed formation of benzene-fused pyrrolizinones **19** from *N*-(2-alkynylphenyl)-β-lactams **18** has been accomplished (Scheme 10). Platinum was

the metal of choice, being gold salts less effective [51]. This cycloisomerization can be viewed as a net intramolecular insertion of one end of the alkyne into the lactam amide bond with concurrent migration of the substituent at the alkyne terminus. It was proposed an initial *5-endo-dig* cyclization of the lactam nitrogen to the metal-activated alkyne followed by the fragmentation of the lactam amide bond and the formation of an acyl cation.

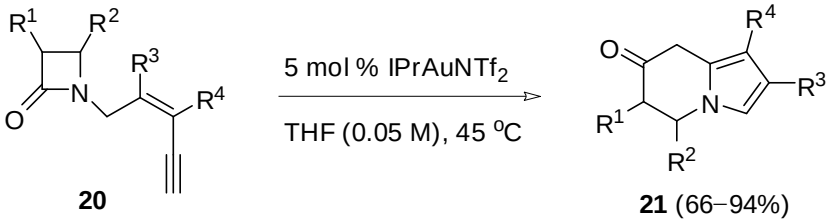


18 **19** (67–99%)

Scheme 10: Precious metal-catalyzed formation of cyclopentanone-fused indoles from *N*-(2-alkynylphenyl)-β-lactams.

The above chemistry was extended to nonaromatic substrates, providing a new approach to other *N*-heterocycles [52]. Thus, the benzene ring was substituted by a *cis*-alkene, and a gold-catalyzed synthesis of 5,6-dihydro-8*H*-indolizin-7-ones **21** from *N*-(pent-2-en-4-ynyl)-β-lactams **20** was developed (Scheme 11). Pt(II) and Pt(IV) also catalyzed this reaction albeit less efficiently. In this reaction, a *5-exo-dig* cyclization of the β-lactam nitrogen to the Au-activated C–C triple bond is followed by heterolytic fragmentation of the amide bond, forming a reactive acyl cation. While substrates with substituents at the alkyne terminus did not undergo this catalytic reaction, various substituents at the C–C double bond were tolerated, including benzoxyethyl and cyclohexyl (geminal to the ethynyl group) as well as hexyl and phenyl (vicinal to the lactam), leading to dihydroindolizinones with different substitutions at their 1- and 2-positions. Substrates with the C–C double bond embedded in medium-sized rings

also reacted well, yielding interesting seven-/eight-membered ring fused dihydroindolizinones in good yields. Surprisingly, the corresponding cyclopentene or cyclohexene substrates did not afford the corresponding five-/six-membered ring-fused dihydroindolizinones, and the starting materials were mostly unreacted for the former and partly decomposed for the later after 10 h. This method allows an expedient formal synthesis of indolizidine 167B.



20 **21** (66–94%)

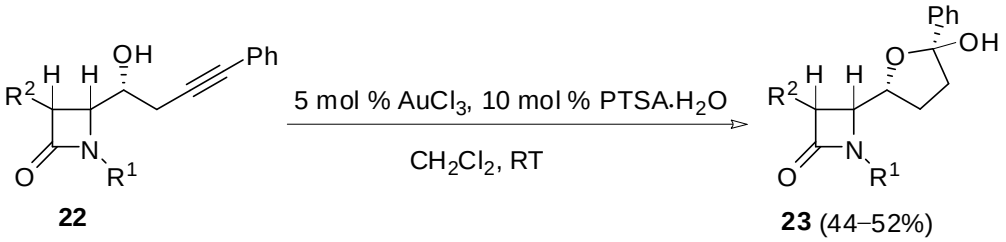
Scheme 11: Gold-catalyzed formation of 5,6-dihydro-8*H*-indolizin-7-ones from *N*-(pent-2-en-4-ynyl)-β-lactams.

Oxycyclizations

Transition metal-assisted intramolecular addition of oxygen nucleophiles across a carbon–carbon triple bond is intriguing from the point of view of regioselectivity as well as it being one of the most rapid and convenient methods for the preparation of oxacycles [53–64]. However, the gold-catalyzed cycloisomerization and tandem oxycyclization/hydroxylation of 2-azetidinone-tethered alkynols for the synthesis of non-fused, spiranic, and fused oxabicyclic β-lactams have been just recently reported [65].

Attempts of a cyclization reaction of terminal alkynols using gold catalysts failed. Fortunately, it was found that under the appropriate reactions conditions $AuCl_3$ could be a good catalyst for the cycloetherification reaction of non-terminal alkynols **22**. Examples in Scheme 12 show that tetrahydrofuryl hemiacetals **23** are accessible as

single isomers in fair yields through the gold-catalyzed tandem oxycyclization/hydroxylation reaction of 2-azetidinone-tethered homopropargylic alcohols. In the conversion from alkynols **22** to tetrahydrofuryl hemiacetals **23**, water is required. Probably, it comes from the trace amount of water present in the solvent or the catalyst. Additionally, it should be noted that PTSA has water in it and the monohydrate is actually employed.

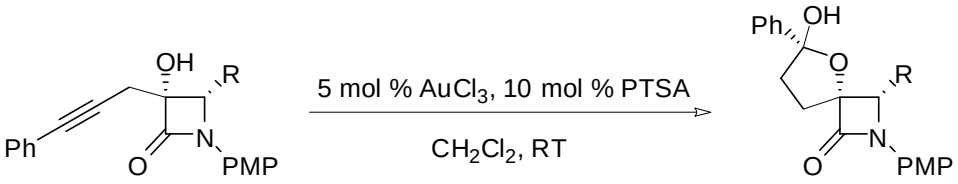


22 **23** (44–52%)

Scheme 12: Gold-catalyzed formation of non-fused tetrahydrofuryl β-lactam hemiacetals from 2-azetidinone-tethered homopropargylic alcohols.

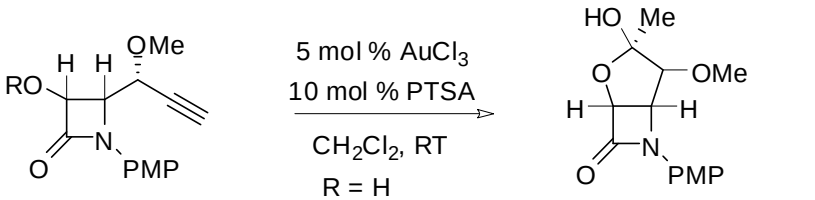
In order to determine whether the conclusions with homopropargylic alcohols **22** could be extrapolated to other alkynols, tertiary carbinols **24** were examined. Under similar gold-catalyzed conditions, spiro β-lactams **25** were obtained as single isomers in good yields (Scheme 13). To further probe the scope of these transformations, the tolerance of the gold-catalyzed heterocyclization reactions of alkynols to the fused bicyclic version was also tested. Indeed, treatment of 2-azetidinone-tethered bishomopropargylic alcohol **26** with $AuCl_3$ provided the desired cycloetherification/hydroxylation product **27** in good yield (Scheme 14). Interestingly, the gold-catalyzed reaction of **28** possessing a (methoxymethyl)oxy moiety instead the free hydroxyl group, also proceeded smoothly to give the cyclization product **27** albeit in lower yield (Scheme 14). Notably, the observed regioselectivity (5-*exo* cyclization) was not affected by the presence of a protective group at the hydroxyl moiety. These gold-catalyzed oxycyclizations were successfully extended to

trishomopropargylic alcohol **29**, yielding the oxycyclization/hydroxylation adduct **30** with concomitant MOM cleavage (Scheme 14). By contrast, the presence of a phenyl substituent at the terminal alkyne carbon showed a substantial effect on the reactivity, as illustrated by the fact that phenyl alkynol **31** did afford a complex mixture.



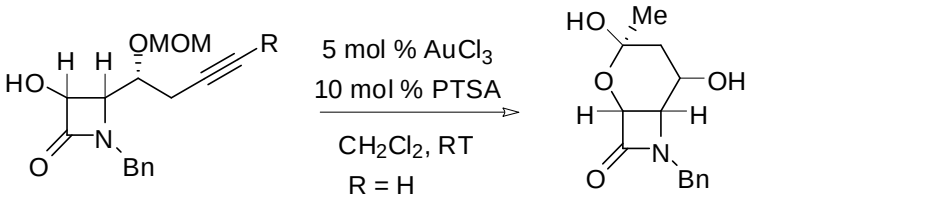
24 **25** (50–67%)

Scheme 13: Gold-catalyzed formation of spiranic tetrahydrofuryl β-lactam hemiacetals from 2-azetidinone-tethered homopropargylic alcohols.



26 R = H
28 R = MOM

27 R = H (59%)
27 R = MOM (46%)



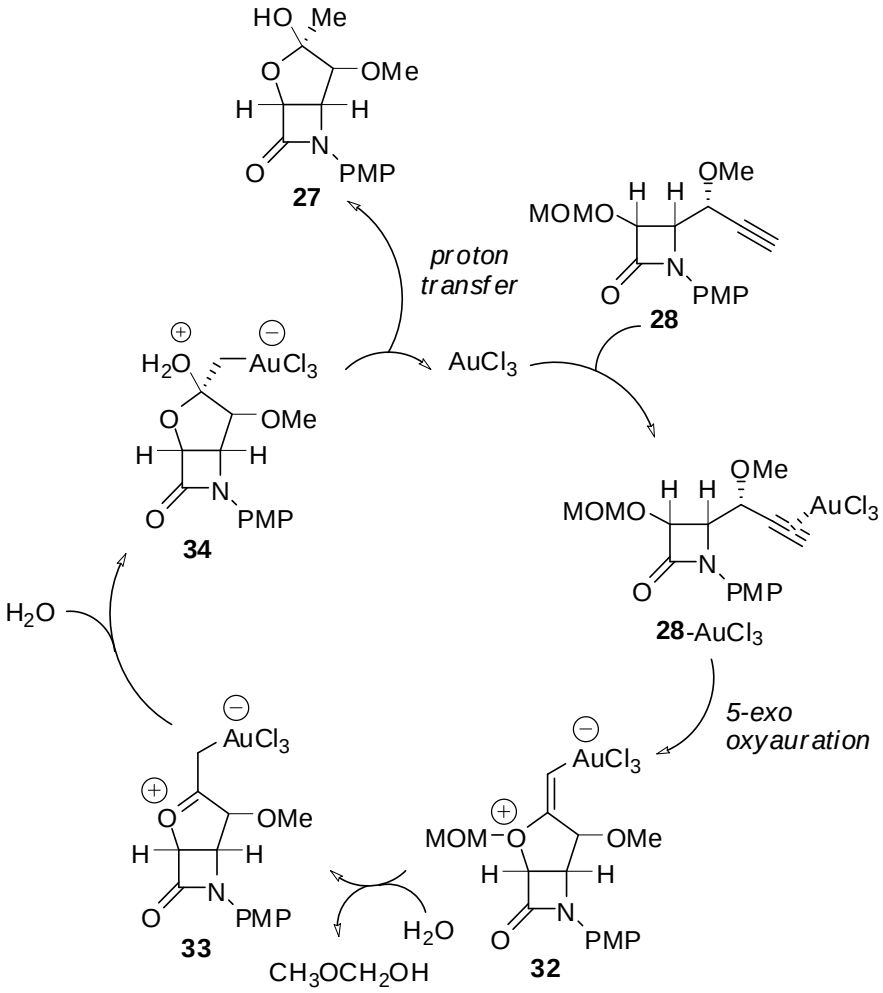
29 R = H
31 R = Ph

30 R = H (81%)
30 R = Ph (complex mixture)

Scheme 14: Gold-catalyzed formation of fused tetrahydrofuryl β-lactam hemiacetals from 2-azetidinone-tethered bis- and tris-homopropargylic alcohols.

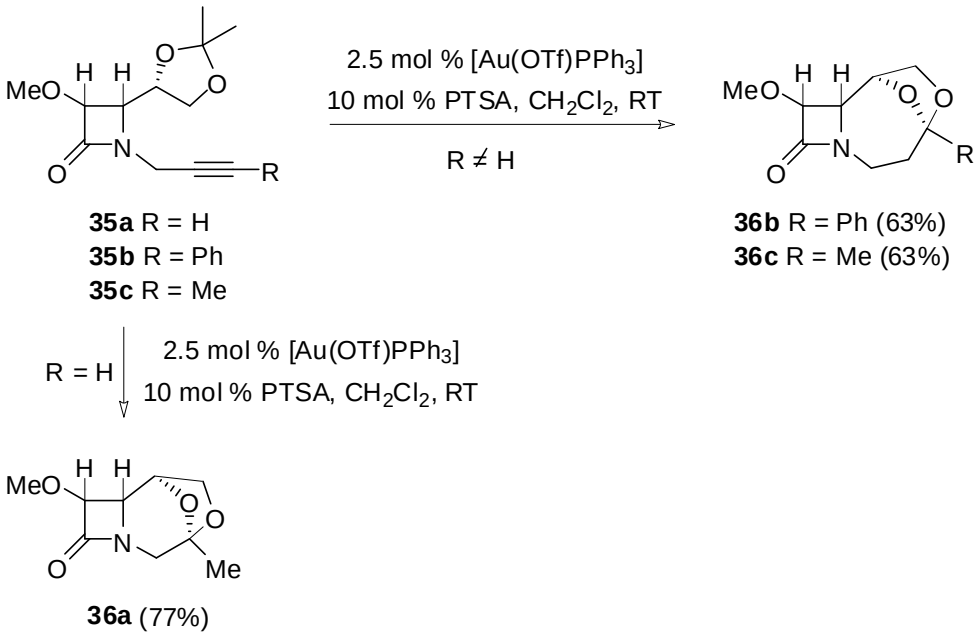
A conceivable mechanism for the achievement of bicyclic tetrahydrofuran **27** from the methoxymethyl ether **28** may initially involve the formation of a π-complex **28**-$AuCl_3$ through coordination of the gold trichloride to the alkyne moiety. Next, it could be

presumed that the initially formed alkynegold complex **28**-$AuCl_3$ undergoes a regioselective intramolecular attack (5-*exo* versus 6-*endo* oxyauration) by the (methoxymethyl)oxy group giving rise to the vinylgold intermediate **32**, which linked to an elimination of methoxymethanol would then isomerizes to the metalaoxocarbenium species **33**. Probably, the water molecule in the third step of the catalytic cycle comes from the trace amount of water present in the solvent or the catalyst. Subsequent nucleophilic attack of water from the less hindered face of intermediate **33** would form the ate complex **34**. Deauration linked to proton transfer liberate adduct **27** with concomitant regeneration of the Au(III) species (Scheme 15).



Scheme 15: Possible catalytic cycle for the gold-catalyzed cyclization of MOM protected alkynol derivatives.

Regiocontrolled gold/Brønsted acid co-catalyzed direct bis-heterocyclization of alkynyl-β-lactams allows the efficient synthesis of optically pure tricyclic bridged acetals bearing a 2-azetidinone nucleus [66–67]. Using the terminal alkyne **35a**, the catalytic system $AuCl_3$/PTSA gave the desired ketal **36a** accompanied by appreciable amounts of a polar ketone, arising from alkyne hydration. Fortunately, the [$AuClPPh_3$]/AgOTf/PTSA system demonstrated better activity. Interestingly, in contrast to the precious metal/acid-cocatalyzed reaction of terminal alkynyl dioxolane **35a** which lead to the 6,8-dioxabicyclo[3.2.1]octane derivative **36a** (proximal adduct), the reaction of substituted at the terminal end alkynyl dioxolanes **35b** and **35c** under identical conditions gave the 7,9-dioxabicyclo[4.2.1]nonane derivatives **36b** and **36c** (distal adducts) as the sole product (Scheme 16), through an exclusive 7-*endo*/5-*exo* bis-oxycyclization by initial attack of the oxygen atom to the external alkyne carbon. The competition between the initial 6-*exo* and 7-*endo* oxycyclizations is gained by the latter, despite *a priori* should be energetically more demanding.



35a R = H
35b R = Ph
35c R = Me

36b R = Ph (63%)
36c R = Me (63%)

36a (77%)

Scheme 16: Gold/Brønsted acid co-catalyzed formation of bridged β-lactam acetals from 2-azetidinone-tethered alkynyldioxolanes.

Conclusion

In summary, regiocontrolled gold-catalyzed heterocyclization reactions of 2-azetidinone-tethered allenes and alkynes leading to a variety of oxa- and azacycles have been developed. Density functional theory (DFT) calculations were performed to obtain insight on various aspects of this reactivity, showing the selective activation of the allene and alkyne component.

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References

1. Satoh, T.; Tsurugi, H.; Miura, M. *Chem. Rec.* **2008**, *8*, 326.

2. Patil, N. T.; Yamamoto, Y. *Arkivoc* **2007**, *(v)*, 6.

3. Severin, R.; Doye, S. *Chem. Soc. Rev.* **2007**, *36*, 1407.

4. Nevado, C.; Echavarren, A. M. *Synthesis* **2005**, 167.

5. Krause, N.; Winter, C. *Chem. Rev.* **2011**, *111*, 1994.

6. Cumulenes and Allenes, *Science of Synthesis, Houben-Weyl Method of Molecular Transformation*, vol. 44, Krause, N., Ed.; George Tieme, Sttutgart, 2007.

7. Ma, S. *Chem. Rev.* **2005**, *105*, 2829.

8. *Modern Allene Chemistry*, Krause, N.; Hashmi, A. S. K., Eds.; Wiley-VCH, Weinheim, 2004.

9. Zimmer, R.; Dinesh, C. U.; Nandanan, E.; Khan, F. A. *Chem. Rev.* **2000**, *100*, 3067.

10. Hashmi, A. S. K. *Angew. Chem. Int. Ed.* **2010**, *49*, 5232.

11. Lipshutz, B.; Yamamoto, Y. Eds.; *Chem. Rev.* **2008**, *108*, special issue 8.

12. Hutchings, G. J.; Brust, M.; Schmidbaur, H. Eds.; *Chem. Soc. Rev.* **2008**, *37*, special issue 9.

13. Corma, A.; Leyva-Pérez, A.; Sabater, M. J. *Chem. Rev.* **2011**, *111*, 1657.

14. Hashmi, A. S. K.; Hutchings, G. J. *Angew. Chem. Int. Ed.* **2006**, *45*, 7896.

15. Muzart, J. *Tetrahedron* **2008**, *64*, 5815.

16. Hashmi, A. S. K. *Chem. Rev.* **2007**, *107*, 3180.

17. Niccolai, D.; Tarsi, L.; Thomas, R. J. *Chem. Commun.* **1997**, 2333.

18. Southgate, R. *Contemp. Org. Synth.* **1994**, *1*, 417.

19. Southgate, R.; Branch, C.; Coulton, S.; Hunt, E. In *Recent Progress in the Chemical Synthesis of Antibiotics and Related Microbial Products*; Lukacs, G. Ed., Springer: Berlin, 1993; vol. 2, pp. 621.

20. Veinberg, G.; Vorona, M.; Shestakova, I.; Kanepe, I.; Lukevics, E. *Curr. Med. Chem.* **2003**, *10*, 1741.

21. Clader, J. W. *J. Med. Chem.* **2004**, *47*, 1.

22. Kvaerno, L.; Ritter, T.; Werder, M.; Hauser, H.; Carreira, E. M. *Ang. Chem. Int. Ed.* **2004**, *43*, 4653.

23. Rothstein, J. D.; Patel, S.; Regan, M. R.; Haenggeli, C.; Huang, Y. H.; Bergles, D. E.; Jin, L.; Hoberg, M. D.; Vidensky, S.; Chung, D. S.; Toan, S. V.; Bruijn, L. I.; Su, Z.-z.; Gupta, P.; Fisher, P. B. *Nature* **2005**, *433*, 73.

24. Alcaide, B.; Almendros, P.; Aragoncillo, C. *Chem. Rev.* **2007**, *107*, 4437.

25. Deshmukh, A. R. A. S.; Bhawal, B. M.; Krishnaswamy, D.; Govande, V. V.; Shinkre, B. A.; Jayanthi, A. *Curr. Med. Chem.* **2004**, *11*, 1889.

26. Alcaide, B.; Almendros, P. *Synlett* **2002**, 381.

27. Palomo, C.; Aizpurua, J. M.; Ganboa, I.; Oiarbide, M. *Synlett* **2001**, 1813.

28. Alcaide, B.; Almendros, P. *Chem. Soc. Rev.* **2001**, *30*, 226.

29. Alcaide, B.; Almendros, P. *Curr. Med. Chem.* **2004**, *11*, 1921.

30. Alcaide, B.; Almendros, P. *Curr. Org. Chem.* **2002**, *6*, 245.

31. Lee, P. H.; Kim, H.; Lee, K.; Kim, M.; Noh, K.; Kim, H.; Seomoon, D. *Angew. Chem. Int. Ed.* **2005**, *44*, 1840.

32. Morita, N.; Krause, N. *Org. Lett.* **2004**, *6*, 4121.

33. Morita, N.; Krause, N. *Eur. J. Org. Chem.* **2006**, 4634.

34. Hashmi, A. S. K.; Ramamurthi, T. D.; Rominger, F. *Adv. Synth. Catal.* 2010, **352**, 971.

35. Hashmi, A. S. K.; Döpp, R.; Lothschütz, M. R.; Riedei, D.; Rominger, F. *Adv. Synth. Catal.* 2010, **352**, 1307.

36. Liu, L. P.; Hammond, G. B. *Chem. Asian J.* **2009**, *4*, 1230.

37. Hashmi, A. S. K.; Schuster, A. M.; Rominger, F. *Angew. Chem. Int. Ed.* **2009**, *48*, 8247.

38. Correa, A.; García-Mancheño, O.; Bolm, C. *Chem. Soc. Rev.* **2008**, *37*, 1108.

39. Díaz, D. D.; Miranda, P. O.; Padrón, J. I.; Martin, V. S. *Curr. Org. Chem.* **2006**, *10*, 457.

40. Bolm, C.; Legros, J.; Le Paih, J.; Zani, L. *Chem. Rev.* **2004**, *104*, 6217.

41. Alcaide, B.; Almendros, P.; Martínez del Campo, T. *Chem. Eur. J.* **2008**, *14*, 7756.

42. Hoffmann-Röder, A.; Krause, N. *Org. Lett.* **2001**, *3*, 2537.

43. Krause, N.; Hoffmann-Röder, A.; Canisius, J. *Synthesis* **2002**, 1759.

44. Deutsch, C.; Gockel, B.; Hoffmann-Röder, A.; Krause, N. *Synlett* **2007**, 1790.

45. Zhang, Z.; Liu, C.; Kinder, R. E.; Han, X.; Qian, H. Widenhoefer, R. A. *J. Am. Chem. Soc.* **2006**, *128*, 9066.

46. Zhang, Z.; Widenhoefer, R. A. *Angew. Chem. Int. Ed.* **2007**, *46*, 283.

47. Hamilton, G. L.; Kang, E. J.; Mba, M.; Toste, F. D. *Science* **2007**, *317*, 496.

48. Alcaide, B.; Almendros, P.; Martínez del Campo, T. *Angew. Chem. Int. Ed.* **2007**, *46*, 6684.

49. Alcaide, B.; Almendros, P.; Martínez del Campo, T.; Soriano, E.; Marco-Contelles, J. L. *Chem. Eur. J.* **2009**, *15*, 1901.

50. Alcaide, B.; Almendros, P.; Martínez del Campo, T.; Soriano, E.; Marco-Contelles, J. L. *Chem. Eur. J.* **2009**, *15*, 1909.

51. Li, G.; Huang, X.; Zhang, L. *Angew. Chem. Int. Ed.* **2008**, *47*, 346.

52. Peng, Y.; Yu, M.; Zhang, L. *Org. Lett.* **2008**, *10*, 5187.

53. Dzudza, A. ; Marks, T. J. *Chem. Eur. J.* **2010**, *16*, 5148.

54. We, L.; Cui, L.; Zhang, G.; Zhang, L. *J. Am. Chem. Soc.* **2010**, *132*, 3258.

55. Belot, S.; Quintard, A.; Krause, N.; Alexakis, A. *Adv. Synth. Catal.* **2010**, *352*, 667.

56. Weyrauch, J. P.; Hashmi, A. S. K.; Schuster, A.; Hengst, T.; Schetter, S.; Littmann, A.; Rudolph, M.; Hamzic, M.; Visus, J.; Rominger, F.; Frey, W.; Bats, J. W. *Chem. Eur. J.* **2010**, *16*, 956.

57. Alemán, J.; del Solar, V.; Navarro-Ranninger, C. *Chem. Commun.* **2010**, *46*, 454.

58. Wang, Y.; Xu, L.; Ma, D. *Chem. Asian J.* **2010**, *5*, 74.

59. Wilckens, K.; Uhlemann, M.; Czekelius, C. *Chem. Eur. J.* **2009**, *15*, 13323.

60. Hashmi, A. S. K.; Schuster, A. M.; Rominger, F. *Angew. Chem.* **2009**, *121*, 8396.

61. Barluenga, J.; Fernández, A.; Diéguez, A.; Rodríguez, F.; Fañanás, F. J. *Chem. Eur. J.* **2009**, *15*, 11660.

62. Chung, Y. K.; Fu, G. C. *Angew. Chem.* **2009**, *121*, 2259.

63. Meng, J.; Zhao, Y.-L.; Ren, C.-Q.; Li, Y.; Li, Z.; Liu, Q. *Chem. Eur. J.* **2009**, *15*, 1830.

64. Arimitsu, S.; Hammond, G. B. *J. Org. Chem.* **2007**, *72*, 8559.

65. Alcaide, B.; Almendros, P.; Martínez del Campo, T.; Carrascosa, R. *Eur. J. Org. Chem.* **2010**, 4912.

66. Alcaide, B.; Almendros, P.; Carrascosa, R.; Torres, M. R. *Adv. Synth. Catal.* **2010**, *352*, 1277.

67. Alcaide, B.; Almendros, P.; Carrascosa, R. *Chem. Eur. J.* **2011**, *17*, 4968.

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